

CLAIMS:

1. A cell targeting conjugate comprising the following components that are covalently conjugated via a linker that is degradable within the target cells:

5 i) a DNA minor groove binding ligand incorporating an effective Auger electron-emitting and/or gamma-emitting and/or positron-emitting atom or photoactive moiety;

 ii) a target cell specific protein or peptide that is capable of internalisation by target cells.

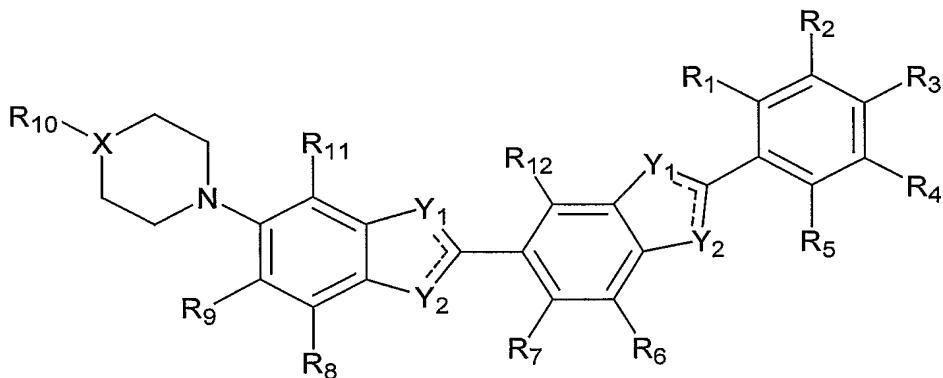
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2. The cell targeting conjugate according to claim 1 wherein the linker comprises a hydrazone, and/or disulphide and/or amide bond.

15 3. The cell targeting conjugate according to either claim 1 or claim 2 wherein the DNA minor groove binding ligand is selected from lexitropsins, bibenzimidazoles, tribenzimidazoles, benzoxazoles, benzthiazoles, purines, DAPI, diarylamidines, SN series ligands, pentamidine analogues, CC1065, naturally occurring antibiotics; and analogues thereof.

20 4. The cell targeting conjugate according to any one of claims 1 to 3 wherein the target cell specific protein or peptide is selected from anti-A33, C595, 4D5, trastuzumab (Herceptin), egf/R3, humanized h-R3, C225 (Erbitux), BrE-3, murine A7, C50, humanized MN-14, anti-A33, MSN-1, bivatuzumab, U36, KIS1, HuM195, anti-CD45, anti-CD19, TXU(anti-CD7)-pokeweed antiviral protein, M195, anti-CD23, apolizumab (Hu1D10),
25 Campath-1H, N901, Ep2, somatostatin analogues, tosimumomab (Bexxar), ibritumomab tiuxetan (Zevalin), HB22.7, anti-CD40, OC125, PAM4 and J591.

30 5. The cell targeting conjugate according to any one of claims 1 to 4 wherein the cell targeting conjugate is represented by Formula (I), wherein:



Formula (I)

X is carbon or nitrogen;

Y₁ and Y₂ are selected from C(R'), nitrogen, N(R'), oxygen and sulfur, wherein R' is hydrogen, optionally substituted alkyl or optionally substituted alkenyl, and wherein Y₁ and Y₂ are not both either C(R') or nitrogen;

— is a double bond unless the attached Y₁ or Y₂ is N(R'), oxygen or sulfur in which case it is a single bond;

R₁ to R₁₂ are selected from hydrogen, halogen, hydroxy, amino, optionally substituted alkyl, optionally substituted alkenyl, a moiety including a target cell specific protein or peptide, an Auger electron-emitting moiety, a gamma-emitting moiety, a positron-emitting moiety, a photoactive moiety and a cellular uptake inhibiting group, and wherein two of R₁ to R₅ may together form optionally substituted cycloalkyl, cycloalkenyl or aryl; wherein at least one of R₁ to R₁₂ comprises a target cell specific protein or peptide, and wherein at least one other of R₁ to R₁₂ comprises an Auger electron-emitting moiety, a gamma-emitting moiety, a positron-emitting moiety and/or a photoactive moiety;

and salts thereof, pharmaceutically acceptable derivatives thereof, pro-drugs thereof and/or

tautomers thereof.

6. A method of selectively eliminating target cells comprising administering to an environment in which the target cells are located an effective amount of a cell targeting

conjugate, comprising the following components that are covalently conjugated via a linker that is degradable within the target cells:

- i) a DNA minor groove binding ligand incorporating a cytotoxically effective Auger electron emitting atom;
- 5 ii) a target cell specific protein or peptide that is capable of internalisation by the target cells.

7. A method of selectively eliminating target cells comprising administering to an environment in which the target cells are located an effective amount of a cell targeting 10 conjugate, comprising the following components that are covalently conjugated via a linker that is degradable within the target cells:

- i) a DNA minor groove binding ligand incorporating a photoactive moiety which when photoactivated generates a species that induces cytotoxic DNA damage;
- 15 ii) a target cell specific protein or peptide that is capable of internalisation by the target cells;

and exposing the target cells to a source of UV light suitable to initiate formation of the species that induces cytotoxic DNA damage.

20 8. A method of selectively imaging target cells comprising administering to an environment in which the target cells are located an effective amount of a cell targeting conjugate, comprising the following components that are covalently conjugated via a linker that is degradable within the target cells:

- i) a DNA minor groove binding ligand incorporating a gamma-emitting and/or positron-emitting atom;
- 25 ii) a target cell specific protein or peptide that is capable of internalisation by the target cells;

and detecting and imaging gamma and/or positron emissions from the target cells.

30 9. The method according to any one of claims 6 to 8 wherein the cell targeting conjugate is administered to an ex-vivo population of cells.

10. The method according to any one of claims 6 to 8 wherein the cell targeting conjugate is administered to a mammalian patient.

5 11. The method according to any one of claims 6 to 10 wherein the target cells are tumour cells.

12. The method according to any one of claims 6 to 11 wherein the linker comprises a hydrazone, and/or disulphide and/or amide bond.

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13. The method according to any one of claims 6 to 12 wherein the target cell specific protein or peptide is selected from anti-A33, C595, 4D5, trastuzumab (Herceptin), egf/R3, humanized h-R3, C225 (Erbitux), BrE-3, murine A7, C50, humanized MN-14, anti-A33, MSN-1, bivatuzumab, U36, KIS1, HuM195, anti-CD45, anti-CD19, TXU(anti-CD7)-15 pokeweed antiviral protein, M195, anti-CD23, apolizumab (Hu1D10), Campath-1H, N901, Ep2, somatostatin analogues, tositumomab (Bexxar), ibritumomab tiuxetan (Zevalin), HB22.7, anti-CD40, OC125, PAM4 and J591.

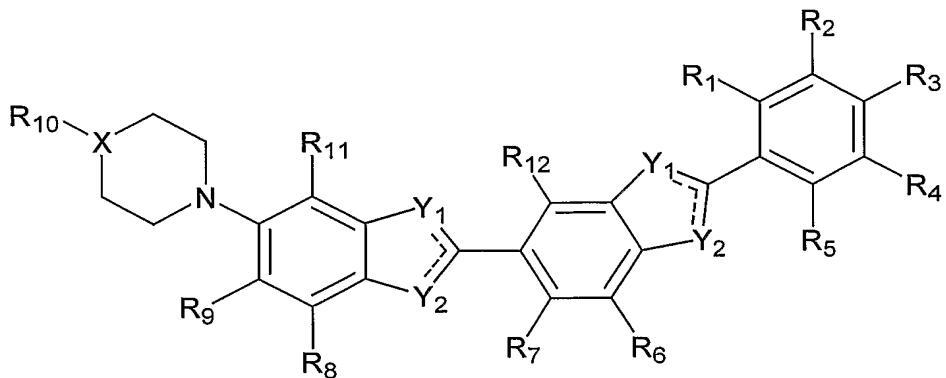
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14. The method according to any one of claims 6 to 13 wherein the DNA minor groove binding ligand is selected from lexitropsins, bibenzimidazoles, tribenzimidazoles, benzoxazoles, benzthiazoles, purines, DAPI, diarylamidines, SN series ligands, pentamidine analogues, CC1065, naturally occurring antibiotics; and analogues thereof.

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15. The method according to any one of claims 6 to 13 wherein the cell targeting conjugate is represented by Formula (I), wherein:

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Formula (I)

X is carbon or nitrogen;

Y_1 and Y_2 are selected from $\text{C}(\text{R}')$, nitrogen, $\text{N}(\text{R}')$, oxygen and sulfur, wherein R' is hydrogen, optionally substituted alkyl or optionally substituted alkenyl, and wherein Y_1 and Y_2 are not both either $\text{C}(\text{R}')$ or nitrogen;

— is a double bond unless the attached Y_1 or Y_2 is $\text{N}(\text{R}')$, oxygen or sulfur in which case it is a single bond;

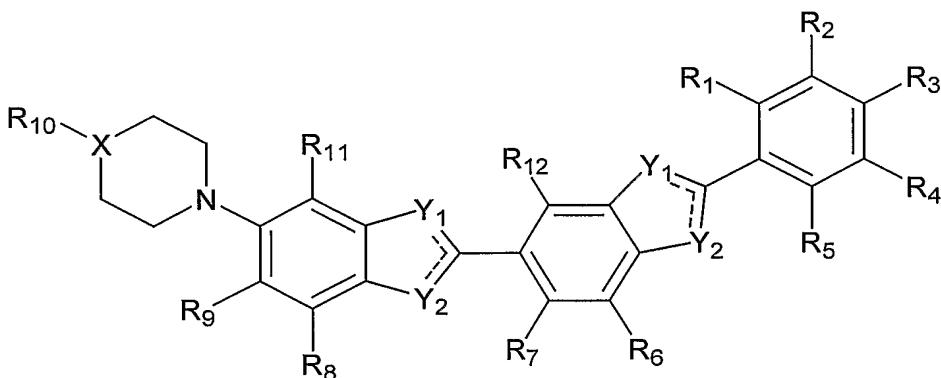
R_1 to R_{12} are selected from hydrogen, halogen, hydroxy, amino, optionally substituted alkyl, optionally substituted alkenyl, a moiety including a target cell specific protein or peptide, an Auger electron-emitting moiety, a gamma-emitting moiety, a positron-emitting moiety, a photoactive moiety and a cellular uptake inhibiting group, and wherein two of R_1 to R_5 may together form optionally substituted cycloalkyl, cycloalkenyl or aryl; wherein at least one of R_1 to R_{12} comprises a target cell specific protein or peptide, and wherein at least one other of R_1 to R_{12} comprises an Auger electron-emitting moiety, a gamma-emitting moiety, a positron-emitting moiety and/or a photoactive moiety;

and salts thereof, pharmaceutically acceptable derivatives thereof, pro-drugs thereof and/or tautomers thereof.

16. The method according to claim 8 wherein the gamma-emitting and/or positron-emitting atom is distanced from a DNA minor groove binding region of the conjugate.

17. A compound according to Formula (I) wherein:

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Formula (I)

X is carbon or nitrogen;

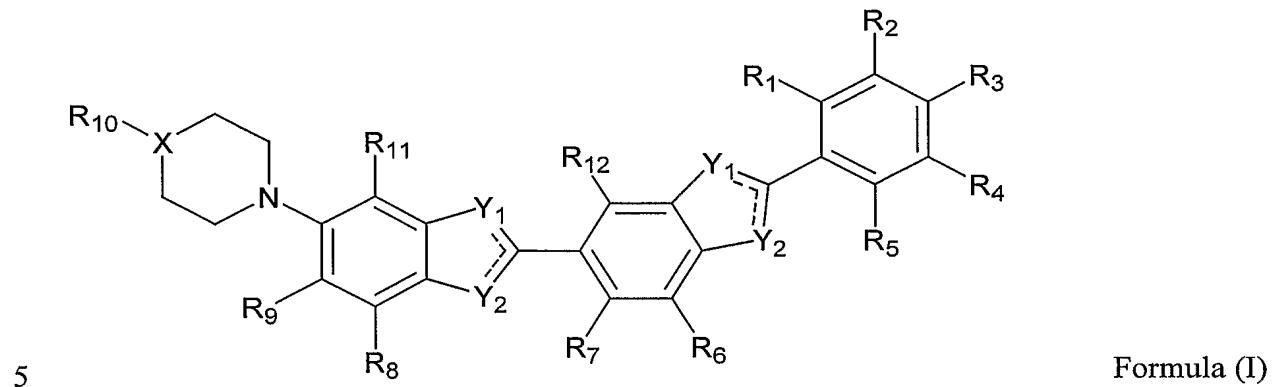
Y₁ and Y₂ are selected from C(R'), nitrogen, N(R'), oxygen and sulfur, wherein R' is hydrogen, optionally substituted alkyl or optionally substituted alkenyl, and wherein Y₁ and Y₂ are not both either C(R') or nitrogen;

— is a double bond unless the attached Y₁ or Y₂ is N(R'), oxygen or sulfur in which case it is a single bond;

R₁ to R₁₂ are selected from hydrogen, halogen, hydroxy, amino, optionally substituted alkyl, optionally substituted alkenyl, a leaving group, an activating group, a chelating group and a cellular uptake inhibiting group, and wherein two of R₁ to R₅ may together form optionally substituted cycloalkyl, cycloalkenyl or aryl; wherein at least one of R₁ to R₁₂ comprises a carbonyl, carboxylic acid or amino group, and wherein at least one other of R₁ to R₁₂ comprises a leaving group, an activating group or a chelating group;

and salts thereof, pharmaceutically acceptable derivatives thereof, pro-drugs thereof and/or tautomers thereof.

18. A compound according to Formula (I) wherein:



X is carbon or nitrogen;

Y₁ and Y₂ are selected from C(R'), nitrogen, N(R'), oxygen and sulfur, wherein R' is hydrogen, optionally substituted alkyl or optionally substituted alkenyl, and wherein Y₁ and Y₂ are not both either C(R') or nitrogen;

— is a double bond unless the attached Y₁ or Y₂ is N(R'), oxygen or sulfur in which case it is a single bond;

15 R₁ to R₁₂ are selected from hydrogen, halogen, hydroxy, amino, optionally substituted alkyl, optionally substituted alkenyl, an Auger electron-emitting moiety, a gamma-emitting moiety, a positron-emitting moiety, a photoactive moiety and a cellular uptake inhibiting group, and wherein two of R₁ to R₅ may together form optionally substituted cycloalkyl, cycloalkenyl or aryl; wherein at least one of R₁ to R₁₂ comprises a carbonyl, carboxylic acid or amino group, and wherein at least one other of R₁ to R₁₂ comprises an Auger electron-emitting moiety, a gamma-emitting moiety, a positron-emitting moiety or a photoactive moiety;

20 and salts thereof, pharmaceutically acceptable derivatives thereof, pro-drugs thereof and/or tautomers thereof.